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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/611,531	06/30/2003	Subramanian S. Venkatraman	ARC 2869 N1	2177

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EXAMINER	
GHALI, ISIS A D	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 05/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/611,531	VENKATRAMAN ET AL.	
	Examiner	Art Unit	
	Isis Ghali	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2006*.

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-33 and 54-57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-33 and 54-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The receipt is acknowledged of applicants' request for RCE and amendment, both filed 02/27/2006.

Claims 1-11, 34-53 have been previously canceled.

Claim 57 is currently added.

Claims 12-33 and 54-57 are pending and included in the prosecution.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 02/27/2006 has been entered.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 12-33, 54 and 55 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 12 and 55 are amended to recite "melt blendable polymer consisting essentially of polyurethane", and the amendment has introduced new matter to the claims because of the following reasons: first, applicants disclosed melt blended mixture of polyurethane polymer and drug, and not melt blendable polymer only with no drug, and secondly, applicants disclosed polyurethane polymer and not polymer consisting essentially of polyurethane that interpreted as polymer blend contains polymers other than polyurethane. Therefore, applicants have no support for, first, "melt blendable polymer" but have support for "melt blend of polyurethane and drug", secondly, applicants have no support for "polymer consisting essentially of polyurethane" but have support for "polyurethane polymer".

The amendment to the claims to recite "even without organic solvent" has introduced new matter because applicants disclosed "without organic solvent" on page 8, lines 3 and 15, and on page 9, line 13. Nowhere applicants have disclosed "even

without". Therefore applicants have support for "without organic solvent" and not for "even without organic solvent".

In accordance to MPEP 714.02, applicant should specifically point out to where in the disclosure a support for any amendment made to the claims can be found.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 12-33, and 54-57 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 12-33 and 54-57 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: after melt bending the polymer and the drug. Applicants recite that the melt blending results in the drug reservoir, while the melt blending results in mixture that is used for drug reservoir or rate controlling membrane for transdermal drug delivery devices, page 9, lines 15-16.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 12-14, 20, 22, and 54 are rejected under 35 U.S.C. 102(b) as being anticipated by US 4,840,796 ('796).

US '796 disclosed a transdermal drug delivery system comprising a backing layer, a matrix containing medicinally active ingredient, and a layer for affixing the system to the skin of the patient (abstract). The matrix is made of polyurethane polymer having melting point at low temperature between 45^0 C to 160^0 C (col.2, lines 53-55; col.4, lines 3-7, 11). The medicinal ingredient or drug is present in concentration between 1-10 wt.% (col.8, Table II). The drug is admixed into molten polymer (col.3, lines 55-59). The matrix may contain material that controls the release rate of the drug from the matrix (col.3, lines 67-68; col.4, lines 1-2).

8. Claims 12, 13, 15-20, 22, 33, and 54 are rejected under 35 U.S.C. 102(b) as being anticipated by 4,638,043 ('043).

US '043 discloses a transdermal drug releasing patch that is non-toxic, non-carcinogenic and biocompatible, oxygen and water vapor permeable, flexible, and can incorporate a wide variety of drugs for a controlled, sustained release to the wearer (abstract; col.2, lines 56-57). The patch comprises support layer, i.e. backing layer (12); a polymer layer of polyurethane containing a drug (16) and a pressure sensitive adhesive layer to fix the patch to the skin (18), i.e. maintaining the patch in drug transmitting relationship with the body surface (col.2, lines 13-22; col.4, lines 45-57;

figures 2 and 3). The drug is contained in an amount of 1-10% in the polyurethane layer and includes analgesics (col.2, line 31; col.3, lines 59-60). The drug and a material that aids in the transport of the drug into the skin, i.e. permeation enhancer, are blended into the polyurethane layer (col.4, lines 1-7). The drug containing layer is made of polyurethane comprises the reaction product of dicyclohexyl methane diisocyanate, polytetramethylene ether polyol, and 1,4-butane diol which is TECOFLEX^{R} (col.8, lines 56-65). The polyurethane polymer is liquid at room temperature to facilitate admixture of drug to form a homogenous blend, and this implies that the melt temperature of the polyurethane is below 100^{0} C and the drug can be blended into the polymer at this temperature (col.2, lines 42-46). The polyurethane polymer does not contain any solvents (col.3, lines 32-33). The modulus of the melt-blended mixture claimed in claim 33 is inherent to specific polymer and specific drug.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 12-20, 22, 33, and 54 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,638,043 ('043).

US '043 teaches a transdermal drug releasing patch that is non-toxic, non-carcinogenic and biocompatible, oxygen and water vapor permeable, flexible, and can incorporate a wide variety of drugs for a controlled, sustained release to the wearer (abstract; col.2, lines 56-57). The patch comprises support layer, i.e. backing layer (12); a polymer layer of polyurethane containing a drug (16) and a pressure sensitive adhesive layer to fix the patch to the skin (18), i.e. maintaining the patch in drug transmitting relationship with the body surface (col.2, lines 13-22; col.4, lines 45-57; figures 2 and 3). The drug is contained in an amount of 1-10% in the polyurethane layer and includes analgesics (col.2, line 31; col.3, lines 59-60). The drug and a material that aids in the transport of the drug into the skin, i.e. permeation enhancer, are blended into the polyurethane layer (col.4, lines 1-7). The drug containing layer is made of polyurethane comprises the reaction product of dicyclohexyl methane diisocyanate, polytetramethylene ether polyol, and 1,4-butane diol (col.8, lines 56-65). The polyurethane polymer is liquid at room temperature to facilitate admixture of drug to

form a homogenous blend, i.e. below 100^0 C (col.2, lines 42-46). The polyurethane polymer does not contain any solvents that may hinder the effectiveness of many drugs (col.3, lines 32-33).

However, US '043 does not explicitly teach that the process temperature and the modulus of the polyurethane polymer. The process temperature and the modulus of the polyurethane polymer disclosed by US '043 are expected to be the same as instantly claimed because the reference teaches the same polymer formed from the same polymer reaction that is liquid at room temperature, i.e. below 100^0 C but does not specify temperature between 40^0 C and 90^0 C.

The temperature between 40^0 C and 90^0 C does not impart patentability to the claims absent evidence to the contrary.

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal drug delivery patch comprising a polyurethane polymer layer containing a drug wherein the polyurethane layer is liquid at room temperature and contains no solvents as disclosed by US '043, and adjust the temperature to that required to melt the drug into the liquid polyurethane polymer according to specific drug used without the use of any solvents, motivated by the teaching of US '043 that the absence of solvent is advantageous because solvents hinder the effectiveness of many drugs, with reasonable expectation of having transdermal drug delivery patch containing polyurethane polymer layer that is non-toxic and biocompatible produced without using any solvents at a temperature below 100^0 C,

thus, reserving the drug effectiveness and providing the maximum desired effect to the patient.

12. Claims 12-33, 54-57 rejected under 35 U.S.C. 103(a) as being unpatentable over US '043 in view of US 5,273,757 ('757) or *vise versa*.

The teachings of US '043 are discussed above. US '043 does explicitly teach that the process temperature and the modulus of the polyurethane polymer. US '043 does not teach specific drugs and permeation enhancer and the amounts of all the ingredients. US '043 does not teach the acrylate adhesive in skin contact layer.

The specific drugs and enhancers as well as amounts of different ingredients do not impart patentability to the claims, absent evidence to the contrary.

The acrylate adhesive is known as skin contact layer, its instant use does not impart patentability to the claims, absent evidence to the contrary.

US '757 teaches transdermal drug delivery device suitable to deliver drug to the skin comprises backing layer, and hot melt adhesive layer comprising 10-100% polyurethane adhesive, 10-80% plasticizer such as fatty acid esters, and drug such as fentanyl (abstract; col.col.3, lines 25-30, 54; col.4, lines 6-9, 39-43). The hot melt adhesive layer has process temperature between 40^0 C and 80^0 C and does not contain any solvent therefore the process is advantageous manner for less temperature-sensitive substances because no toxic solvent residues can remain in the transdermal patch, less time consuming, less environmental polluting, and coast saving (col.2, lines 54-61; col.4, lines 43-54).

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal drug delivery device that has matrix formed of melt blend of polyurethane, active agent and permeation enhancer as disclosed by US '043, and use a temperature process between 40^0 C and 80^0 C and fentanyl as an active agent, and fatty acid ester as an enhancer as disclosed by US '757, motivated by the teaching of US '757 that process temperature between 40^0 C and 80^0 C without solvent is advantageous manner for less temperature-sensitive substances because no toxic solvent residues can remain in the transdermal patch, less time consuming, less environmental polluting, and coast saving, with reasonable expectation of having transdermal drug delivery device that has matrix comprising melt blend of polyurethane, fentanyl, and fatty acid ester that is processed at 40^0 C and 80^0 C without solvent that is advantageously prepared in a manner suitable for less temperature-sensitive substances, not toxic, less time consuming, less environmental polluting, and coast saving, and meanwhile deliver fentanyl effectively in enhanced manner to the skin of the patient in need of such treatment.

Vise versa, US '757 does not teach the skin contact layer of the transdermal device or the specific starting material for the polyurethane.

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal device to deliver fentanyl comprising matrix of polyurethane having a process temperature between 40^0 C and 80^0 C without solvent as disclosed by US '757, and add the skin contact layer to protect the matrix as disclosed by US '043, and replace the polyurethane by the polyurethane produces by

the reaction product of dicyclohexyl methane diisocyanate, polytetramethylene ether polyol, and 1,4-butane diol as disclosed by US '043, motivated by the teaching of US '043 that such polyurethane is non-toxic, non-carcinogenic and biocompatible, oxygen and water vapor permeable, flexible, and provides a controlled, sustained release of the drug to the wearer, with reasonable expectation of having a matrix comprising fentanyl, fatty acid enhancer, and polyurethane produces by the reaction product of dicyclohexyl methane diisocyanate, polytetramethylene ether polyol, and 1,4-butane diol that is non-toxic, non-carcinogenic and biocompatible, oxygen and water vapor permeable and flexible that provides controlled, sustained release of fentanyl to the wearer.

13. Claims 21, 28, 29 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over US '043 in view of US '757 and further in view of US '6,139,866 ('866).

The combined teachings of US '043 and US '757 are discussed above.

The combination of US '043 with any of US '757 does not specifically teach the glycerol monolaurate permeation enhancer, or acrylate adhesive as skin contact layer.

US '866 teaches percutaneous formulation to deliver fentanyl wherein the formulation is stable and has little irritation to the skin and excellent in percutaneous permeation of fentanyl (abstract). The formulation comprises 0.05-20% of fentanyl, 0.1-98% of pressure sensitive adhesive that can be acrylate adhesive, and 0.01-20% of permeation enhancer such as glycerol monolaurate which has recognized absorption

enhancing effect on the skin (col.1, lines 65-67; col.2, lines 1-2, 67; col.4, lines 9-11, 28-31, 37-39).

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal drug delivery device that has matrix formed of melt blend of polyurethane, fentanyl and fatty acid permeation enhancer as disclosed by US '043 combined with US '757, and replace the permeation enhancer by glycerol monolaurate and further use acrylate as skin contact adhesive as disclosed by US '866, motivated by the teaching of US '866 such a percutaneous formulation comprising glycerol monolaurate and acrylate adhesive delivers fentanyl with little irritation to the skin and provides excellent recognized percutaneous permeation, with reasonable expectation of having a transdermal melt blend matrix comprising polyurethane, fentanyl and glycerol monolaurate and acrylate skin contact layer wherein the device has excellent permeation to fentanyl without skin irritation.

14. Claims 21, 28 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over US '043 in view of US '757, and further in view of US 5,066,648 ('648).

The combined teachings of US '043 and US '757 are discussed above.

The combination of US '043 with US '757 does not specifically teach lauryl pyroglutamate as a permeation enhancer.

US '648 teaches pryoglutamic acid esters as safe dermal permeation enhancers being capable of improving delivery of active agent through the skin and into the general

circulation and undergo fast metabolic breakdown into non-toxic metabolic products as soon as they reach the live area of the skin (abstract; col.3, lines 25-42).

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal drug delivery device that has matrix comprising melt blend of polyurethane, fentanyl and permeation enhancer as disclosed by US '043 in combination with US '757, and replace the enhancer by pyroglutamic acid esters as disclosed by US '648, motivated by the teaching of US '648 that pryoglutamic acid esters are safe dermal permeation enhancers capable of improving delivery of active agent through the skin and into the general circulation and undergo fast metabolic breakdown into non-toxic metabolic products as soon as they reach the live area of the skin, with reasonable expectation of having a transdermal device that deliver fentanyl from a melt blend matrix comprising polyurethane and lauryl pyroglutamate with improved permeation of fentanyl to the circulation without causing any toxic effects.

15. Claim 32 is rejected under 35 U.S.C. 103(a) as being unpatentable over US '043 in view of US '757, and further in view of US 5,599,648 ('289).

The combined teachings of US '043 and US '757 are discussed above.

The combination of US '043 with any of US '757 does not specifically teach the skin contact adhesive as acrylate adhesive.

US '289 teaches wound dressing comprising skin contact acrylate adhesive layer that is preferred because it is hypoallergenic and non-irritating to the skin (col.5, lines 35-39, 45-49).

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal drug delivery device that has matrix formed of melt blend of polyurethane and fentanyl, and skin contact layer as disclosed by US '043 in combination with US '757, and use acrylate adhesive to form the skin contact layer as disclosed by US '289, motivated by the teaching of US '289 that acrylate adhesive layer is preferred because it is hypoallergenic and non-irritating to the skin, with reasonable expectation of having transdermal drug delivery device that has matrix formed of melt blend of polyurethane and fentanyl, and comprising an acrylate adhesive skin contact layer that can be worn by the patient without causing irritation or allergic reaction, thus, delivers the active agent comfortably to the user.

Response to Arguments

16. Applicant's arguments with respect to claims 12-33 and 54-57 have been considered but are moot in view of the new ground(s) of rejection.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis Ghali whose telephone number is (571) 272-0595. The examiner can normally be reached on Monday-Thursday, 7:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Isis Ghali
Examiner
Art Unit 1615

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